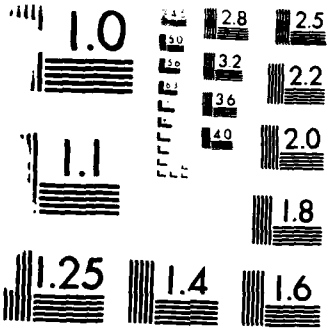
AD-A165 042 SECONDARY FREE RADIAL INTERMEDIATES IN THE SYNTHESIS OF 1/1
2-METHYL-6-NITROINDAZOLE(U) NAVAL RESEARCH LAB
WASHINGTON DC J H BOYER ET AL. 10 MAR 86 NRL-MR-5736

UNCLASSIFIED F/G 7/3 NL



(2)

NRL Memorandum Report 5736

Secondary Free Radical Intermediates in the Synthesis of 2-Methyl-6-Nitroindazole

J. H. BOYER,* M. D. PACE, P. PAGORIA,* T. P. PILLAI,* AND D. STEC†

Polymeric Materials Branch
Chemistry Division

**University of New Orleans*
Department of Chemistry
New Orleans, LA 70148

†Geo-Centers, Inc.
Wharton, NJ 07885

March 10, 1986

NAVAL RESEARCH LABORATORY
Washington, D.C.

AD-A165042

SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

1a. REPORT SECURITY CLASSIFICATION UNCLASSIFIED	1b. RESTRICTIVE MARKINGS
2a. SECURITY CLASSIFICATION AUTHORITY	3 DISTRIBUTION / AVAILABILITY OF REPORT Approved for public release; distribution unlimited.
2b. DECLASSIFICATION / DOWNGRADING SCHEDULE	
4. PERFORMING ORGANIZATION REPORT NUMBER(S) NRL Memorandum Report 5736	5. MONITORING ORGANIZATION REPORT NUMBER(S)
6a. NAME OF PERFORMING ORGANIZATION Naval Research Laboratory 6b. OFFICE SYMBOL (If applicable) Code 6122	7a. NAME OF MONITORING ORGANIZATION
6c. ADDRESS (City, State, and ZIP Code) Washington, DC 20375-5000	7b. ADDRESS (City, State, and ZIP Code)
8a. NAME OF FUNDING / SPONSORING ORGANIZATION Office of Naval Research 8b. OFFICE SYMBOL (If applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER
8c. ADDRESS (City, State, and ZIP Code) Arlington, VA 22217	10. SOURCE OF FUNDING NUMBERS PROGRAM ELEMENT NO. 61153N; PROJECT NO.; TASK NO. RR013-06-4F; WORK UNIT ACCESSION NO. DN280-038

11. TITLE (Include Security Classification)
Secondary Free Radical Intermediates in the Synthesis of 2-Methyl-6-Nitroindazole

12. PERSONAL AUTHOR(S)
Boyer, J.H.,* Pace, M.D., Pagoria, P.,* Pillai, T.P.,* and Stec, D.†

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Year, Month, Day)	15. PAGE COUNT
Interim	FROM 11/84 TO 11/85	1986 March 10	14

16. SUPPLEMENTARY NOTATION
*University of New Orleans, Department of Chemistry, New Orleans, LA 70148
†Geo-Centers, Inc., Wharton, NJ 07885

17 COSATI CODES		
FIELD	GROUP	SUB-GROUP

18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
EPR
Free radicals
2-Methyl-6-nitroindazole

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

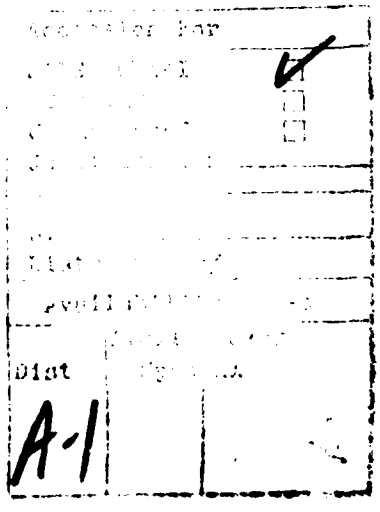
Four distinct free radical intermediates were detected by electron spin resonance (e.s.r.) spectroscopy during the spontaneous conversion of an isomeric mixture of 2,4 and 3,4-dinitro-N,N-dimethylbenzylamine to 2-methyl-6-nitroindazole. These spectra include an iminoxyl radical, R-N*N-O· (not reproducible); a dimethylnitroxyl radical, $(CH_3)_2NO\cdot$ (reproducible); and two structurally unidentified radicals (also reproducible). Free radical intermediates were detected only when the reaction was started by nitrating 4-nitro-N,N-dimethylbenzylamine. No free radicals were detected when the reaction was started by mixing separately prepared 2,4 and 3,4-dinitro-N,N-dimethylbenzylamine. (3,4-dinitro-N,N-dimethylbenzylamine alone does not convert to 2-methyl-6-nitroindazole).

20 DISTRIBUTION / AVAILABILITY OF ABSTRACT ☒ UNCLASSIFIED/UNLIMITED ☐ SAME AS RPT ☐ DTIC USERS	21 ABSTRACT SECURITY CLASSIFICATION UNCLASSIFIED
22a. NAME OF RESPONSIBLE INDIVIDUAL M. D. Pace	22b TELEPHONE (Include Area Code) (202) 767-3239 22c. OFFICE SYMBOL Code 6122

DD FORM 1473, 84 MAR 83 APR edition may be used until exhausted
All other editions are obsolete

SECURITY CLASSIFICATION OF THIS PAGE

CONTENTS



Secondary Free Radical Intermediates in the Synthesis of 2-methyl-6-nitroindazole

I. INTRODUCTION

The chemistry of nitro and nitroso groups is important in synthetic routes to new energetic materials. The synthesis of 2-methyl-6-nitroindazole by two methods (both requiring cyclization involving a nitro group) has been reported.[1] The mechanism of formation was shown to require basic conditions and was suggested to involve an N-oxide intermediate. The synthesis of 2-methyl-6-nitroindazole from 4-nitro-N,N-dimethylbenzylamine as the starting material was performed. The final reaction product was monitored by electron spin resonance (e.s.r.) and nuclear magnetic resonance (n.m.r.) spectroscopies during a time period of several weeks. Free radical intermediates were detected when the reaction was started by nitrating 4-nitro-N,N-dimethylbenzylamine to form an isomeric mixture of 2,4 and 3,4-dinitro-N,N-dimethylbenzylamine. No free radicals were detected when the reaction was started by mixing separately prepared 2,4-dinitro-N,N-dimethylbenzylamine and 3,4-dinitro-N,N-dimethylbenzylamine.

II. RESULTS AND DISCUSSION

An isomeric mixture composed of 2,4-dinitro-N,N-dimethylbenzylamine (II) and 3,4-dinitro-N,N-dimethylbenzylamine (III) is produced by nitration of 4-nitro-N,N-dimethylbenzylamine (I) as shown in equation (1). The dominant isomer is the 2,4-isomer. Proton nmr spectra of these isomers show different chemical shifts. For 2,4-dinitro-N,N-dimethylbenzylamine the peak assignments are: a singlet peak at δ=2.43 for $-CH_2-$ and a singlet peak at δ=3.78 for $-(CH_3)_2$. For 3,4-dinitro-N,N-dimethylbenzylamine the peak assignments are: a singlet peak at δ=3.88 for $-CH_2-$ and a singlet peak at δ=2.32 for $-(CH_3)_2$. The conversion of 2,4-dinitro-N,N-dimethylbenzylamine into 2-methyl-6-nitroindazole requires ca. 2 months (as determined by proton and C-13 n.m.r. spectra). A solution of the 2,4 isomer (in acetonitrile) was found to convert into the indazole more slowly than a solution composed of an equimolar mixture of 2,4 isomer and 3,4 isomer. In further studies we found that dimethylbenzylamine itself catalyzes the conversion suggesting that the catalysis is due to the basic properties of the added material. We also found that the addition of

Manuscript approved November 20, 1985.

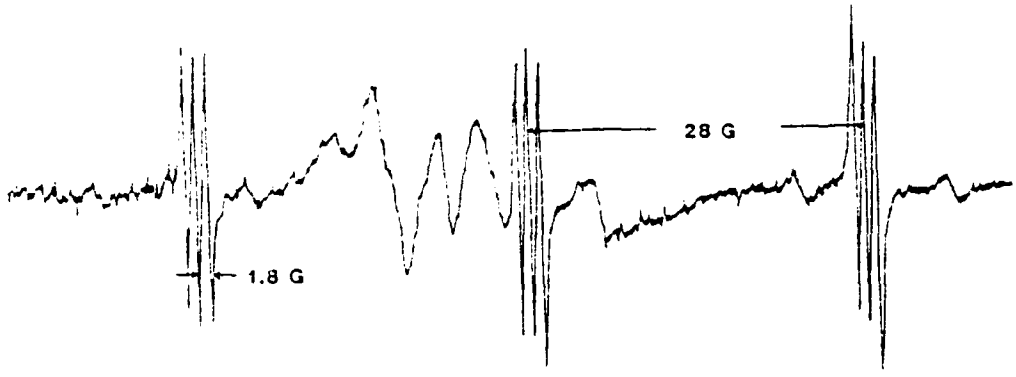


Fig. 1. The first derivative e.s.r. spectrum of an iminoxy radical is shown. The spectrum is composed of 9 lines. A second free radical signal is also recorded.

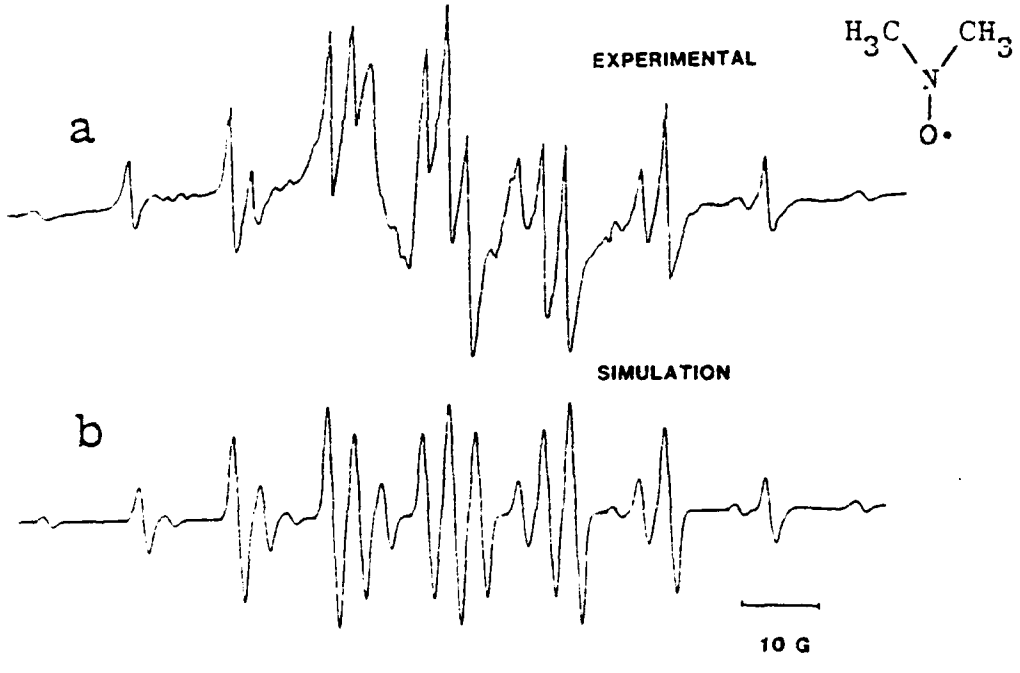
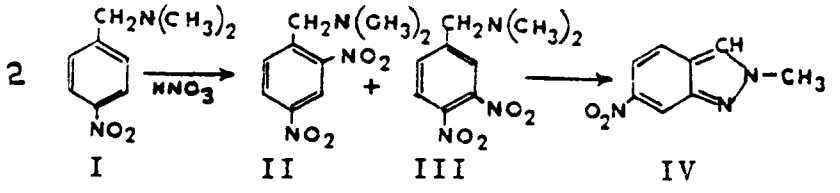


Fig. 2. The first derivative e.s.r. spectrum of a dimethyl nitroxyl radical is shown. This spectrum remains stable for ca. 30 minutes. A simulated spectrum using the couplings listed in the text is shown for comparison.

electron acceptors tetracyanoethylene (TCNE) and dicyano-dichlorobenzoquinone (DDQ) inhibited the conversion to the indazole (after 12 days proton n.m.r. indicated only the presence of the starting 2,4-derivative). A $CDCl_3$ solution of the 2,4-derivative and the electron acceptor is a dark red color. A solution of 3,4 isomer does not convert to indazole.



I II III IV

equation (1)

2-methyl-6-nitroindazole

Analysis of the Esr Spectra

Free radicals were detected at sequential time periods during the conversion of the isomeric solution mixture to final indazole product (when the reaction was started by nitration of 4-nitro-N,N-dimethylbenzylamine in equation 1). The first e.s.r. spectrum was recorded following nitration and within 10 minutes after removal of ether from the reaction product (but was not reproducible). Fig. 1 shows the e.s.r. spectrum recorded from an 0.1 ml sample of the reaction product dissolved in acetonitrile. The spectrum shows two different free radical signals. One signal is composed of 9 sharp lines each with a linewidth of 0.5G (G=Gauss). This 9 line spectrum is consistent with a free radical having two inequivalent ^{14}N (I=1) hyperfine couplings. The larger coupling is 28 G. This coupling is assigned to an iminoxy free radical. Iminoxy radicals have ^{14}N coupling values in the range of 28 to 33 G.[2] The smaller coupling of 1.8 G is assigned to the second ^{14}N nucleus. No ^{1}H hyperfine couplings were detected. (^{1}H couplings appear as integral multiples of overlapped doublets usually with large hyperfine couplings for β-protons).[2] Based upon the ^{14}N coupling values the radical having the structure R-N=N-O· is assigned to this spectrum [where R is $O_2N(C_6H_3)CH_2N(CH_3)_2$]. A similar spectrum of the C_6H_5-N=N-O· radical has been reported elsewhere.[3] This radical decays within several seconds and was not always detected during each experimental run.

The intensities of the second set of broad peaks in Fig. 1 continued to increase with time. After ca. 15 minutes the spectrum appeared as shown in Fig. 2a. A computer simulated spectrum of the major spectral component of Fig. 2a is shown in Fig. 2b. This pattern is assigned to two different hyperfine couplings. A 15.6 G coupling is assigned to an

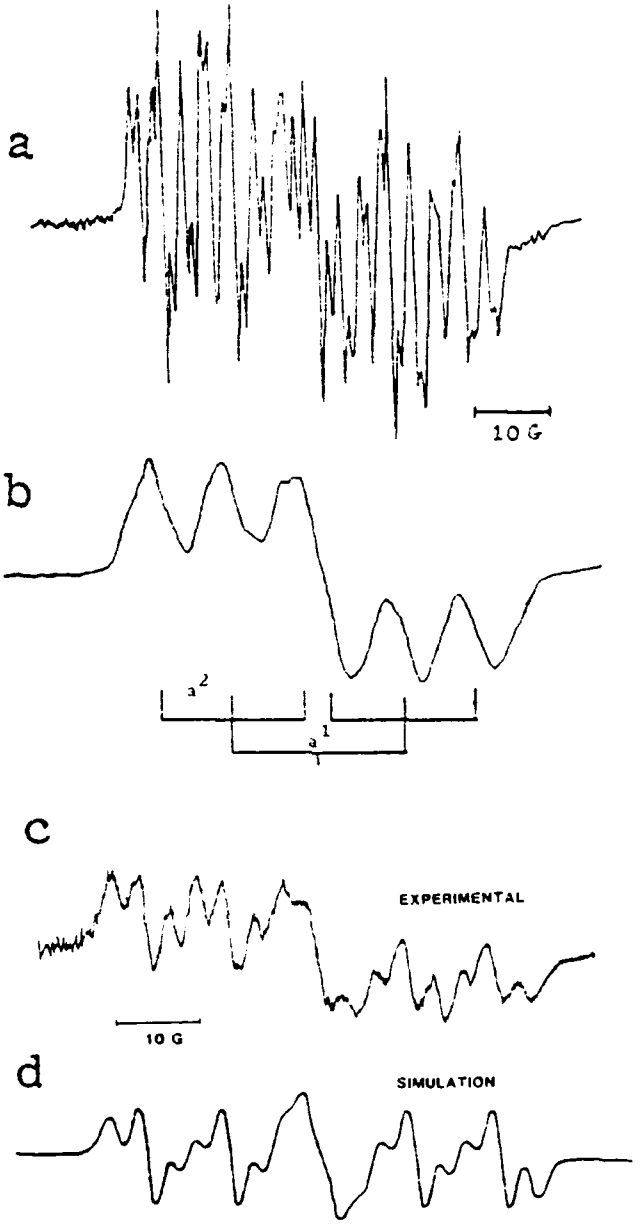


Fig. 3. a) The first derivative spectrum of an overlapping signal from free radicals which remain stable for several days after the synthesis.

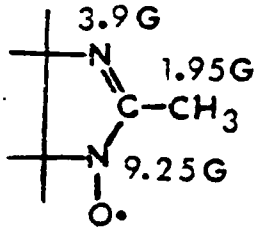
b) The spectrum in a) was recorded by using a modulation amplitude of 5G. This spectrum clearly shows the major couplings.

c) The reaction product was dissolved in CCl_4 and the spectrum of this sample is shown. This spectrum is attributed to a single free radical signal.

d) The spectrum in c) was simulated using the couplings a^1, a^2, and a^3 listed in the text.

^{14}N nucleus and contributes a 1:1:1 triplet splitting. The second coupling of 12.2 G is assigned to 6 equivalent protons which contribute a 7 line splitting with the relative intensity ratios 1:10:15:20:15:10:1. This is consistent with a dimethylnitroxyl radical, $(CH_3)_2NO\cdot$. An equivalent spectrum of this radical has been reported.[4] The dimethylnitroxyl radical is likely formed by dissociation of the benzylic C-N single bond in the amine II and migration of oxygen from the nitro group.

The spectrum in Fig. 2a remained stable for 30 minutes. Afterwards, a different free radical signal, as shown in Fig. 3a, was recorded. (The same spectrum, in Fig. 3b, was recorded by using a Zeeman modulation amplitude of 5 G. Overmodulation, as in Fig. 3b, artifactually broadens the linewidth so that only major spectral couplings are resolved.) Two hyperfine couplings were measured from the modulation broadened spectrum. These couplings are a^1=20.8 G (assigned to a single proton, I = 1/2, coupling) and a^2=9.48 G (assigned to a single ^{14}N, I=1, coupling). Proton couplings can vary an order of magnitude depending upon their proximity to the unpaired electron site.[5] Protons having an isotropic coupling of ca. 20 G can be attributed to α-protons in carbon centered radicals[5] (RR'CH), or α-protons in alkylamino cation radicals[6] ($RR'NH^+$); and β-protons in certain nitroxyl radicals[7] (-CH-N-O·). ^{14}N couplings for nitroxyl radicals usually have a value near 16 G. If the nitroxyl group is adjacent to a conjugated ring (such as a phenyl ring), then the ^{14}N coupling has been reported to range from ca. 9 to 11 G.[3,8] Another example of an ^{14}N coupling having this value has been reported for cyclic imino nitroxyl radicals (having two ^{14}N couplings, e.g. Structure V)[9].

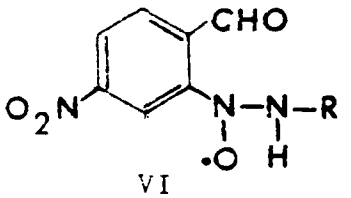


Structure V

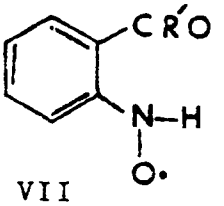
From the high magnetic field and low magnetic field regions of Fig. 3a, two additional couplings were measured. These couplings are a^3=3.06 G (assigned to two equivalent protons) and a^4=1.05 G (assigned to a ^{14}N coupling). Two equivalent protons contribute triplet 1:2:1 intensity ratio to the spectral pattern. A coupling of 3.06 G is common for protons on an aromatic ring which is adjacent to a nitroxyl function.[10] A ^{14}N coupling of 1.05 G is small and occurs for radicals having two adjacent nitrogens. An example has been reported for diazacyclopentadienone anion radicals and for other nitroxyl radicals having adjacent nitrogens.[8,11] A fifth coupling, a^5, was estimated by using computer

simulations of the linewidth and spectral intensities. This coupling is assigned to a proton coupling having a value of 0.6 G. After 5 days the spectrum was recorded showing little change in the relative peak intensities in the high and low magnetic field regions of the spectrum. Differences in peak intensities near the center field region of Fig. 3a indicated an overlapping spectral pattern from other free radical signals. The existence of a broad single line pattern (linewidth of 8 G) overlapping the center field region of the spectrum in Fig. 3a was confirmed by recording a spectrum of this single line radical signal after all other spectral components had decayed (several weeks after the synthesis).

In a separate experiment a substance was extracted from the indazole reaction product mixture and was then dissolved in CCl_4. This gave a spectrum which is attributed to a single radical species (shown in Fig. 3c). The following couplings were assigned to this spectrum: one ^1H coupling equal to 20.8 G; one ^{14}N coupling equal to 9.48 G; and two equivalent ^1H nuclei with a coupling equal to 3.06 G. (These couplings are identical to a^1, a^2, and a^3 measured from Fig. 3a-b.) A computer simulated spectrum based upon these coupling values is shown in Fig. 3d. A suggested assignment based upon the magnitude of these couplings is indicated by Structure VI. A similar free radical has been reported by Janzen, Lai, and Snetty.[12] This structure is shown by VII.



VI

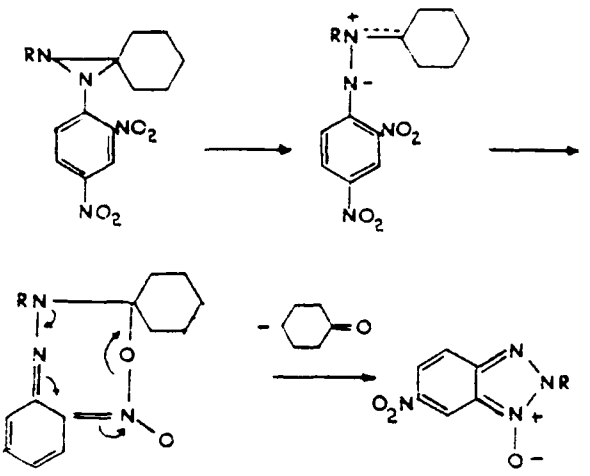


VII

The nitroxyl group ^{14}N couplings in both structures are similar values (9.91 G for VI and 7.93 G for VII), and are both less than the typical nitroxyl coupling value of ca. 15.0 G. Likewise a small proton coupling of ca. 1 to 3 G is attributed to aromatic proton couplings in both structures. Structure VI has a second ^{14}N coupling from the amino alkyl group adjacent to the nitroxyl function. This ^{14}N coupling (1.05 G) is a value similar to previously reported couplings from radicals having adjacent nitrogens.[11] The largest proton coupling in Structure VI (20.3 G) is greater than the α-proton coupling in VII, but within the range of some β-proton couplings. Structure VI is regarded as tentative.

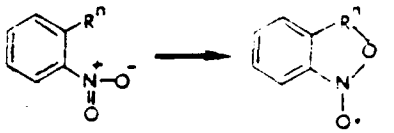
Suggested Mechanism of Cyclization.

Cyclization reactions involving nitro groups occur via formation of both radical and non-radical intermediates. One non-radical example is the conversion of 1-(2,4-dinitrophenyl)-2-methyl-3,3-pentamethylenediaziridine into 2-methyl-6-nitrobenzotriazole-1-oxide.[13]



The possible mechanism, as outlined in reference 13, involves bond formation between an oxygen of the nitro group and a polarized carbon site. This step is followed by elimination of a cyclic ketone to give an -N=N-R functional group which cyclizes with the -N=O function (left from the nitro group) to give the cyclic benzotriazole-oxide.

Cyclizations involving radical intermediates have been reported to involve formation of cyclic alkoxy nitroxyl radicals. This has been shown by intramolecular trapping of β-substituted carbon centered radicals by an ortho-substituted nitro group to form 6-membered ring alkoxy nitroxyl radicals.[14] In another report, the formation of alkoxy nitroxyl radicals was demonstrated from intramolecular trapping of α-alkoxyalkyl radicals by an ortho-nitro group.[12] It has also been shown that benzoyl radicals are capable of abstracting oxygen atoms from an ortho nitro group by a two-step radical addition-cleavage mechanism.[10] These results may be summarized as:



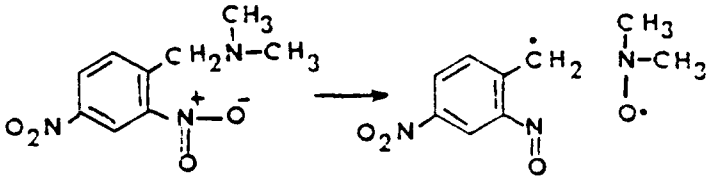
R^1= $-CH_2\dot{C}H_2$

R^2= $-\dot{C}=O$

R^3= 

This overall evidence points to the participation of an oxygen from the nitro group with a reaction center (in the group ortho to the nitro group's location) as a major step toward cyclization.

In this reaction spectral observation of the $(CH_3)_2NO\cdot$ radical indicates such a reaction step. It is not possible to



conclusively link a free radical mechanism to this reaction because the observation of the free radicals requires nitration of 4-nitro-N,N-dimethylbenzylamine as the first reaction step (as shown in equation 1). When the reaction is started by mixing 2,4 and 3,4-dinitro-N,N-dimethylbenzylamine no free radicals are observed.

III. EXPERIMENTAL

Spectra were recorded by using an ER 200 IBM Bruker esr spectrometer. The instrument settings were 20 mw of incident microwave power, 0.63 Gpp of modulation amplitude (at 100 kHz modulation frequency), a 1 sec time constant and a 500 sec scan time with a sweep width of 100 G. ^{13}C and proton nmr spectra of the reaction products were recorded by using a JEOL-PS-100 nmr spectrometer.

2-Methyl-6-nitroindazole, IV:[1] To 8 ml of 65% fuming sulfuric acid, cooled to -5 to 0°C, was added 5 ml 90% fuming nitric acid, dropwise with stirring. The solution was stirred at 25°C for 30 minutes. The solution was cooled to 10°C and

4-nitro-N,N-dimethylbenzylamine (1. g, mol) was added dropwise. After addition the solution was stirred at 25°C for two hours, and then at 50°C for 30 minutes. The reaction mixture was cooled to room temperature, poured onto crushed ice, made basic with Na_2CO_3 (added slowly in small amounts until solution is slightly basic, pH 7 or 8), and extracted with ether (2x100 ml). The combined ether extracts were washed thrice with water, dried (Na_2SO_4). The solvent was removed under vacuum to give a red oil of 2,4-dinitro-N,N-dimethylbenzylamine. This compound slowly converts to 2-methyl-6-nitroindazole.

REFERENCES

1. A. L. Patey and N. M. Waldron, Tetrahedron Lett. 38, 3375 (1970).

2. J. R. Thomas, J. Am. Chem. Soc. 86, 1446 (1964). M. D. Pace and W. B. Moniz, J. Magn. Reson. 43, 240 (1981).

3. W. A. Gibbons and A. M. Trozzolo, J. Am. Chem. Soc., 88, 173 (1966); J.I.G. Cadogan, R. M. Paton, C. Thompson, J. Chem. Soc. (8), 583 (1971).

4. A. Joshi and G. C. Yang, Org. Magn. Reson. 17, 138 (1981).

5. Y. Ellinger, A. Rassat, R. Subra, and G. Berthier, J. Chem. Phys. 58, 2446 (1973).

6. W. C. Danen and R. C. Rickard, J. Am. Chem. Soc. 94, 3254 (1972).

7. E. G. Janzen and J. I.-P. Liu, J. Magn. Reson.9, 510 (1973).

8. S. Terabe and R. Konaka, J. Am. Chem. Soc. 91, 5655 (1969).

9. E. F. Ullman, L. Call, and J. H. Osiecki, J. Org. Chem. 35, 3623 (1970).

10. L. Lunazzi, G. Placucci, and N. Ronchi, J. Chem. Soc., Soc., Perkin Trans. 2, 1132 (1977); E. G. Jansen and U. M. Oehler, Tetrahedron Lett. 24, 669 (1983).

11. G. R. Stevenson, J. F. Hansen, G. Clark, and J. P. Freeman, J. Org. Chem. 44, 3211 (1979).

12. E. G. Janzen, C. C. Lai, and R. V. Shetty, Tetrahedron Lett. 21, 1201 (1980).

13. H. W. Heine, P. G. Williard and T. R. Hoye, J. Org. Chem. 37, 2980 (1972).

14. A.L.J. Beckwith and M.D. Lawton, J. Chem. Soc., Perkin Trans. 2, 2134 (1973).

END

DTIC

FILMED

4-86